

Hepatoblastoma Incidence in the United States From 1973 to 1992

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Background. There is recent evidence to suggest that extremely low birth weight is associated with the occurrence of hepatoblastoma.

Procedure. In light of this possibility, we evaluated trends in hepatoblastoma incidence in the United States among children age 4 years and younger.

Results. We found an increasing trend

(5.2%) in hepatoblastoma incidence over the past two decades, a period that corresponds with improved survival of very low birth weight children.

Conclusion. Future studies of hepatoblastoma that incorporate birth weight are appropriate. *Med. Pediatr. Oncol.* 30:141–142, 1998. © 1998 Wiley-Liss, Inc.

Key words: hepatoblastoma; incidence; trends; United States

INTRODUCTION

Hepatoblastoma is an extremely rare childhood embryonal malignancy, with a reported annual United States incidence rate of approximately 1 per million children under the age of 15 [1]. The malignancy usually presents as an asymptomatic abdominal mass in children younger than three years of age [2]. There have been isolated case reports of hepatoblastoma occurring in association with fetal alcohol syndrome [3], oral contraceptive use during pregnancy [4], and hormonal treatment for sterility [5]. A case-control study conducted by the Children's Cancer Group reported elevated odds ratios with specific parental occupational exposures, including maternal exposures to metals, petroleum products, and paints, and paternal exposures to metals [6]. The etiology of hepatoblastoma, however, is largely unknown.

Recently, investigators in Japan noted that two of their patients with hepatoblastoma were of extremely low birth weight (<1000 grams) [7]. From this observation, Ikeda et al. investigated the birth weights of all children with malignancies registered in the Japan Children's Cancer Registry from 1985–1993. They found that there was a conspicuous over-representation (58% of cases) of hepatoblastoma among children with cancer who were of extremely low birth weight. Over the study period, the authors also noted a statistically significant increase in the percentage of hepatoblastoma patients who weighed less than 1500 grams at birth; no trends toward an increase in the percentage of children with other tumors who weighed less than 1500 grams at birth were observed. Upon further examination, this significant increase in the percentage of hepatoblastoma patients who weighed less than 1500 grams at birth was apparently accounted for by an increase in the number of cases who weighed less than 1000 grams at birth. Although this may be a chance finding, it raises the possibility that factors

associated with prematurity may play a role in the occurrence of hepatoblastoma.

With improved treatments for low birth weight infants over the past few decades, many premature infants are now surviving [8]. It is conceivable that some of the therapies administered in recent years to these very low birth weight infants could be associated uniquely with the development of hepatoblastoma [9]. As a first step toward exploring these associations further, we evaluated changes in hepatoblastoma incidence in the United States over the past two decades.

PROCEDURE

Data on children younger than 5 years of age were abstracted from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. The SEER program collects information on all new occurrences of malignant cancer from population-based cancer registries in several areas of the United States. A standardized, active case-finding procedure is employed at each SEER registry and case ascertainment is estimated at over 96% [10]. This analysis used data from cancer surveillance registries in the following areas: the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah, and the metropolitan areas of Atlanta, Detroit, San Francisco/Oakland, and Seattle/Puget Sound. These ar-

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TABLE I. Incidence Rate and Overall Trends of Hepatoblastoma per Million Children Aged Four Years or Younger

	# of cases	Incidence rate	AAPC*	[95% CL]
Overall (<5 years of age)	124	3.8	5.2	[1.9, 8.6]**
Age at diagnosis				
<1	57	8.7	5.4	[0.5, 10.5]
1	36	5.3	3.7	[-2.2, 10.0]
2	16	2.4	5.7	[-3.4, 15.7]
3	13	2.0	9.4	[-1.5, 21.5]
4	2	0.3	—	
Gender				
Males	69	4.1	2.9	[-1.3, 7.3]**
Females	55	3.4	8.2	[3.0, 13.8]**

*Average annual percent change.

**Adjusted for age.

eas include approximately 10% of the U.S. population. Cases were restricted to children who were newly diagnosed from 1973–1992 with a primary malignant hepatoblastoma (8970/3), International Classification of Diseases for Oncology (ICD-O) [11]. Incidence rates, average annual percentage change (AAPC) of incidence rates, and 95% confidence limits (95% CL) of the AAPC were modeled using Poisson regression [12].

RESULTS

During the period 1973–1992 there was a total of 124 children younger than 5 years of age who were diagnosed with hepatoblastoma, providing an incidence rate of 3.8 per million children aged 4 years or younger (Table 1). Of these children, 75% were diagnosed at age one or younger. There was a notable increase (AAPC = 5.2, 95% CL = 1.9, 8.6) in the incidence of hepatoblastoma diagnosed among children younger than age five years during the study period. There appeared to be no specific age for which this increasing trend was more or less apparent. The incidence of hepatoblastoma was slightly higher in boys, but the increasing secular trend in hepatoblastoma was most notable for girls (AAPC = 8.2; 95% CL = 3.0, 13.8).

CONCLUSIONS

These data suggest that the incidence rate of hepatoblastoma for children younger than age five years has

been increasing in the United States over the past two decades. This result should be interpreted cautiously, however, as the incidence rates and trends are based on very small numbers. This is particularly true for the age-specific rates and trends. The increase in hepatoblastoma incidence coincides with a period of time when there have been marked improvements in survival of low birth weight infants [8]. Due to the ecologic nature of this comparison, however, no causal inferences can be made regarding any association between these two phenomena. Nevertheless, given the suggestive data from Japan, further investigation into the patterns of hepatoblastoma, particularly with regard to birth weight (and perhaps gender) may shed further light on this issue.

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